Docket No.: NEL-0018/NP
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
R. Elaine Fulton et al.

Application No.: 10/784,305 Confirmation No.: 1520

Filed: February 24, 2004 Art Unit: 1648

For: GENETIC ENGINEERING OF STREPTAVIDIN-BINDING PEPTIDE TAGGED SINGLE-CHAIN VARIABLE FRAGMENT ANTIBODY TO VENEZUELAN EQUINE ENCEPHALITIS VIRUS

Examiner: S. B. Chen

RESPONSE TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the Notification of Non-Compliant Appeal Brief dated June 19, 2007, Applicant hereby submits the enclosed second revised Appeal Brief effecting the changes requested in the Notification. More specifically, Applicant has added the claims missing from the revised Appeal Brief filed May 10, 2007 to identify the status of all the claims as per the Examiner's request. Applicant also notes that in Section III, pages 2 and 3 of the original, revised and second revised Appeal Brief, the status of all of the pending claims have been identified.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-0013, under Order NEL-0018/NP from which the undersigned is authorized to draw.

Dated: July 10, 2007

Respectfully submitted,

By_____
Lee Cheng
Registration No.: 40,949
RADER, FISHMAN & GRAUER PLLC
1233 20th Street, N.W. Suite 501
Washington, DC 20036
(202) 955-3750
Attorneys for Applicant

Docket No.: NEL-0018/NP
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
R. Elaine Fulton et al.

Application No.: 10/784,305

Confirmation No.: 1520

Filed: February 24, 2004

Art Unit: 1648

For: GENETIC ENGINEERING OF STREPTAVIDIN-BINDING PEPTIDE TAGGED SINGLE-CHAIN VARIABLE FRAGMENT ANTIBODY TO VENEZUELAN EQUINE ENCEPHALITIS VIRUS

Examiner: S. B. Chen

SECOND REVISED APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

As required under 37 C.F.R. §41.66(a), this brief is filed within the statutory term of the Notice of Appeal filed in this case on October 3, 2006, and is in furtherance of said Notice of Appeal.

The fees required under 37 C.F.R. §41.20(b)(2), and any required petition for extension of time for filing this brief and fees therefor, are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

This brief contains items under the following headings as required by 37 C.F.R. §41.67 and §1205.02 of the MPEP:

I. REAL PARTY IN INTEREST

The real party in interest for this appeal is *Her Majesty the Queen in Right of Canada, as represented by the Minister of National Defence* of Ottawa, Canada. An assignment of all rights in the present application to *Her Majesty the Queen in Right of Canada, as represented by the Minister of National Defence* was executed by the inventor and recorded by the U.S. Patent and Trademark Office at **Reel 015055, Frame 0456.**

II. RELATED APPEALS AND INTERFERENCES

There are no other appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

A. Total Number of Claims in Application

There are 15 total claims in this application.

B. Current Status of Claims

1. Claims canceled: Claims 5 and 6
2. Claims withdrawn from consideration but not canceled: Claims 1-3 and 11-15
3. Claims pending: Claims 1-4 and 7-15
4. Claims allowed: Claims 4 and 7-9
5. Claims rejected: Claim 10

C. Claims on Appeal

The claim on appeal is claim 10.

IV. STATUS OF AMENDMENTS

Applicant filed an Amendment After Final Rejection on August 30, 2006. The Examiner responded to the Amendment After Final Rejection in an Advisory Action mailed September 15, 2006. In the Advisory Action, the Examiner indicated that Applicants' proposed amendments to claim 4 would be entered and would overcome the objection of claims 4 and 7-10 for a minor informality. Having been twice rejected, Applicant filed a Notice of Appeal on October 3, 2006.

Accordingly, the claims enclosed herein as Appendix A incorporates all amendments to claims 1-4 and 7-15 as indicated in the paper filed by Applicant on August 30, 2006.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Claim 4 recites a fusion protein, SBP tagged scFv Ab, comprising a single-chain variable fragment antibody (scFv Ab) fused with a streptavidin-binding peptide (SBP) sequence (see page 7 of the specification). The fusion protein comprises (A) the amino acid sequence encoded by the nucleotide sequence shown in SEQ ID NO: 1 or (B) the amino acid sequence shown in SEQ ID NO: 2 (see Figure 2 of the specification), has a molecular weight of ~32 kDa (see page 13 of the specification), has an antigen-binding affinity to Venezuelan equine encephalitis virus (VEE) (see page 14 of the specification) and has streptavidin-binding activity (see page 7 of the specification). An example of the scFv Ab is a mA116 scFv Ab (see pages 6 and 7 of the specification).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Whether claim 10 can be rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

2. Whether the specification, as amended in Applicant's amendment filed January

23, 2006 can be objected to under 35 U.S.C. §132 for allegedly introducing new matter into the disclosure.

VII. ARGUMENT

In the Office Action of April 4, 2006, the following rejections were presented by the Examiner:

(i) 35 U.S.C. §112, first paragraph

The Examiner rejected claim 10 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Applicant respectfully traverses this rejection.

The Examiner has based this rejection on the position that the specification does not support the monoclonal antibody mA116 as a genus of antibodies. However, Applicant disagrees with the Examiner in this regard.

To satisfy the written description requirement under U.S. practice, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003). Here, in this case, Applicant believes that the claimed invention "*[A] fusion protein, SBP tagged scFv Ab, comprising a single-chain variable fragment antibody (scFv Ab) fused with a streptavidin-binding peptide (SBP) sequence, said fusion protein comprising (A) the amino acid sequence encoded by the nucleotide sequence shown in SEQ ID NO: 1 or (B) the amino acid sequence shown in SEQ ID NO: 2, wherein said scFv Ab is a mA116 scFv Ab*" is described in the specification and claims in sufficient detail **via words and structures** to establish that the inventor had possession of the claimed invention.

First, claim 4 defines the claimed fusion protein as *comprising (A) the amino acid sequence encoded by the nucleotide sequence shown in SEQ ID NO: 1 or (B) the amino acid sequence shown in SEQ ID NO: 2.* Further, claim 10 defines the scFv Ab as a mA116 scFv Ab which according to the description in the "Background of the Invention" section of the

specification, is a ***well characterized*** scFv Ab against VEE based on previously known publications.

Thus, given the examples of mA116 scFv Abs and their respective Deposit Accession Numbers provided by the Applicants, and the teachings of the structures of the claimed fusion protein in the incorporated references, specification and claims, the proper incorporation of which is provided in the arguments section VII (v) below, Applicant believes that they have clearly established possession of the claimed invention.

Applicant also wishes to note that the amendment to claim 10 was presented in the previously filed response to put the claim in better form under U.S. practice by introducing the proper article "*a*" before the newly introduce element of "*mA116 scFv Ab*".

Also, in view of the Examiner's indication that Alvi et al. does provide support for the scFv mA116-6 (see page 4, lines 15-17, of the Advisory Action), Applicant believes that no other remarks need to be submitted with respect to this issue.

Thus, for these reasons, withdrawal of this rejection is respectfully requested.

(ii) 35 U.S.C. §112, second paragraph

None

(iii) 35 U.S.C. §102

None

(iv) 35 U.S.C. §103

None

(v) Other

The Examiner objected to the specification, as amended in Applicant's amendment filed January 23, 2006, under 35 U.S.C. §132 for allegedly introducing new matter into the disclosure. Applicant respectfully traverses this objection.

In support of their amendments to the specification, Applicant noted in the amendment filed January 23, 2006 that the insertion of the examples of mA116 scFv Ab into the specification does not constitute new matter since the disclosure of such antibodies are found in the reference, Alvi AZ, Hu WG, Fulton RE, Nagata LP, Coles JE, and Long MC: *Functional enhancement of a partially active single chain variable fragment antibody to Venezuelan equine encephalitis virus* Viral Immunology 2003; 16:213-222 (see page 2, lines 15-17, of the specification), which has been specifically incorporated by reference (see page 18, lines 1 and 2, of the specification).

The Examiner does not believe that the phrase "*the List of Prior Art Literatures referred to in the Background of the Invention section is incorporated by reference herein*" provide proper support for the legal incorporation of the information described in the prior art literatures. Although the Examiner in the Advisory Action dated September 15, 2006 states "that Applicant's statement on page 18 of the specification expresses a clear intent to incorporate the references listed in the Background section of the specification, including the *Alvi et al.*" reference, such incorporation is impermissible since the mA116 scFv appears to be essential material. Applicant respectfully disagrees with the Examiner in this regard.

As cited by the Examiner, §2163.07 of the Manual of Patent Examining Procedure allows for the incorporation of the content of another document or part thereof by reference to the document in the text of the specification. In other words, the information incorporated is as much a part of the application as filed as if the text was repeated in the application. Thus, replacing the identified material incorporated by reference with the actual text is not new matter.

What constitutes a proper incorporation by reference is defined by 37 C.F.R. §1.57(b) and (c) of the U.S. patent rules, portions of which are reproduced herein below for the Board's convenience.

> *(b) Except as provided in paragraph (a) of this section, an incorporation by reference must be set forth in the specification and must:*
>
> *(1) Express a clear intent to incorporate by reference by using the root words "incorporat(e)" and "reference" (e.g., "incorporate by reference"); and*
>
> *(2) Clearly identify the referenced patent, application, or publication.*
>
> *(c) "Essential material" may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent*

> *application publication, which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material" is material that is necessary to:*
>
> *(1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;*
>
> *(2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or*
>
> *(3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112.*

The Examiner believes that with regard to 37 C.F.R. §1.57(c), Applicant is attempting to incorporate essential materials by reference from a source other than a U.S. patent or U.S. patent Application publication since *Alvi et al.* is only a scientific journal publication. The Examiner believes that the monoclonal antibody mA116 is an essential material because they are required to provide a written description of the claimed invention. However, Applicant believes that the monoclonal antibody mA116 is non-essential material since such antibodies are already well known to one skilled in the art and can be obtained based on the teachings in the art In fact, Applicant has demonstrated the well known and non-essential nature of the monoclonal antibody mA116 by referring to the cited references which provides a written description of the antibody.

More specifically, Applicant clearly presents the citation and teachings of *Alvi et al.* in the Background of the Invention section. On page 6 of the specification, it is stated that "*[T]he present inventors have previously cloned and characterized several single-chain variable fragment antibodies (scFv Abs) against VEE (Alvi et al., 1999; Alvi et al., 2002; Alvi et al., 2003). Among them,* ***mA116 scFv Ab was well characterized****, showing sensitivity and specificity in recognition of VEE by immunoassay (Alvi et al., 2003).*" Applicant believes that such statements in the Background of the Invention section clearly demonstrate that the mA116 scFv Abs are deemed by the inventor to be well known and non-essential material.

Further, Applicant would also like to note that most of these clones have already been disclosed in a U.S. Patent (i.e. U.S. Patent 6,818,748 "*Cloning, Expressions, Sequencing,*

and Functional Enhancement of Monoclonal ScFv Antibody against VEE", issued 16 Nov 2004) which further indicates that the mA116 scFv Abs are deemed by the inventor to be non-essential material.

It should be noted that original claim 4, as originally presented, was directed to a fusion protein, SBP tagged scFv Ab, comprising a single-chain variable fragment antibody (scFv Ab) fused with a streptavidin-binding peptide (SBP) sequence. In other words, the scFv Ab was not limited to the mA116 scFv Ab, even though it was a preferred embodiment of the present invention.

Hence, since mA116 scFv Ab must be deemed to be non-essential material, the insertion of the examples of mA116 scFv Ab into the specification in the Amendment filed January 23, 2006 does not constitute new matter. Thus, for these reasons, withdrawal of this objection is respectfully requested.

The Examiner objected to claims 4 and 7-10 for a minor informality. In the Advisory Action dated September 15, 2006, the Examiner indicated in item 7 of the Action that Applicant's amendment to the claims in the Response filed August 30, 2006 is sufficient to overcome this objection. Thus, Applicant believes that no additional arguments need to be presented in this Appeal Brief since this objection has been indicated by the Examiner to be withdrawn.

VIII. CLAIMS APPENDIX

A copy of the claims involved in the present appeal is attached hereto as Claims Appendix.

IX. EVIDENCE APPENDIX

No evidence pursuant to §§ 1.130, 1.131, or 1.132 or entered by or relied upon by the Examiner is being submitted.

X. RELATED PROCEEDINGS APPENDIX

No related proceedings are referenced in II. above. Thus, no copies of decisions in related proceedings are provided.

Applicant believes that no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-0013, under Order No. NEL-0018/NP from which the undersigned is authorized to draw. Further, Applicant also hereby formally requests rejoinder of method claims 1-3 and 11-15 under *In re* Ochiai upon the allowance of the elected product claims. Applicant has previously amended non-elected claims 1 and 11 to depend on claim 4 to thereby include all the limitations of the allowable product claims in accordance with §821.04 of the MPEP.

Dated: July 10, 2007

Respectfully submitted,

By_____
Lee Cheng
Registration No.: 40,949

RADER, FISHMAN & GRAUER PLLC
1233 20th Street, N.W.
Suite 501
Washington, DC 20036
(202) 955-3750
Attorneys for Applicant

CLAIMS APPENDIX

Claims Involved in the Appeal of Application Serial No. 10/784,305.

1. (Withdrawn) A method for constructing a recombinant gene encoding a single-chain variable fragment antibody cloned into an expression vector and fused with a streptavidin-binding peptide (SBP) gene sequence to produce the SBP tagged recombinant scFv Ab fusion protein of claim 4, said method comprising:

(a) encoding anti-VEE single-chain variable fragment antibody (scFv Ab) gene to a recombinant plasmid and inserting a SBP gene and a 6His tag downstream to develop a SBP tagged scFv Ab construct;

(b) amplifying the resultant scFv/SBP/6His by polymerase chain reaction (PCR);

(c) inserting the amplified PCR products into cloning vector to produce a SBP-plasmid;

(d) constructing said SBP-plasmid with promoter to produce a SBP tagged scFv Ab; and

(e) expressing said SBP tagged scFv Ab in *E. coli* cells as inclusion bodies and purifying the expressed SBP tagged scFv Ab by immobilized metal affinity chromatography to obtain the SBP tagged recombinant scFv Ab fusion protein.

2. (Withdrawn) The method as in claim 1, wherein:

- said recombinant plasmid in step (a) is a pPICZαBmA116 recombinant plasmid;
- said cloning vector in step (c) is pCRT7 TA; and
- said promoter in step (d) is a T7 promoter.

3. (Withdrawn) The method as in claim 1, wherein said anti-VEE scFv Ab is a mA116 Ab.

4. (Previously Presented) A fusion protein, SBP tagged scFv Ab, comprising a single-chain variable fragment antibody (scFv Ab) fused with a streptavidin-binding peptide (SBP)

sequence, said fusion protein comprising (A) the amino acid sequence encoded by the nucleotide sequence shown in SEQ ID NO: 1 or (B) the amino acid sequence shown in SEQ ID NO: 2.

5. (Canceled).

6. (Canceled).

7. (Original) The SBP tagged recombinant scFv Ab fusion protein of claim 4, wherein said fusion protein has a molecular weight of ~32 kDa.

8. (Previously Presented) The SBP tagged recombinant scFv Ab fusion protein of claim 4, wherein said fusion protein has an antigen-binding affinity to Venezuelan equine encephalitis virus (VEE).

9. (Previously Presented) The SBP tagged recombinant scFv Ab fusion protein of claim 4, wherein said fusion protein has streptavidin-binding activity.

10. (Previously Presented) The SBP tagged recombinant scFv Ab fusion protein of claim 4, wherein said scFv Ab is a mA116 scFv Ab.

11. (Withdrawn) A method for detecting VEE, comprising:

(a) reacting the SBP tagged recombinant scFv Ab fusion protein of claim 4 with a sample containing VEE for observing antigen-binding activity; and

(b) analyzing the reactant by enzyme-linked immunosorbent assay (ELISA).

12. (Withdrawn) The method of claim 11, wherein said ELISA immunoassay employs an indicator enzyme and substrate system to visually indicate presence of antigen-binding activity.

13. (Withdrawn) The method of claim 12, wherein horseradish peroxidase is used in said ELISA as the indicator enzyme.

14. (Withdrawn) The method of claim 12, wherein 2,2'-azino-di-(3-ethyl-benzthiazoline-sulfonic acid) diammonium salt (ABTS) is used in said ELISA as the substrate system.

15. (Withdrawn) The method of claim 11, wherein said scFv Ab is a mA116 scFv Ab.

EVIDENCE APPENDIX

NONE

RELATED PROCEEDINGS APPENDIX

NONE